

***Anopheles gambiae*, Anoga-HrTH hormone, free and bound structure – A nuclear magnetic resonance experiment**

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Abstract

The spread of malaria by the female mosquito, *Anopheles gambiae*, is dependent, amongst other things, on its ability to fly. This in turn, is dependent on the adipokinetic hormone, Anoga-HrTH (pGlu-Leu-Thr-Phe-Thr-Pro-Ala-Trp-NH₂). No crystal structure of this important neuropeptide is available and hence NMR restrained molecular dynamics was used to investigate its conformational space in aqueous solution and when bound to a membrane surface. The results showed that Anoga-HrTH has an almost cyclic conformation that is stabilized by a hydrogen bond between the C-terminus and Thr3. Upon docking of the agonist to its receptor, this H-bond is broken and the molecule adopts a more extended structure. Preliminary AKHR docking calculations give the free energy of binding to be -47.30 kJ/mol. There is a close correspondence between the structure of the docked ligand and literature structure–activity studies. Information about the 3D structure and binding mode of Anoga-HrTH to its receptor is vital for the design of suitable mimetics which can act as insecticides.